Smoking Linked to Increased Risk of Pancreatitis

Tolstrup JS, Kristiansen L, Becker U, Grønbaek M. Smoking and risk of acute and chronic pancreatitis among women and men: a population-based cohort study. Arch Intern Med 2009;169:603–9.

Study Overview

Objective. To assess the independent effects of smoking on risk of pancreatitis.

Design. Observational population-based cohort study.

Setting and participants. Participants came from the first 3 examinations of the Copenhagen City Heart Study (CCHS), a prospective cohort study performed in 1976–1978, 1981–1983, and 1991–1994. The CCHS included participants who were randomly chosen from the general population of Copenhagen. Overall, 18,035 individuals participated in 1 or more examinations of the CCHS. For this study, 9573 women and 8332 men with recorded smoking status were followed for a mean of 20.2 years.

Data collection. Subjects completed a self-administered questionnaire regarding smoking, alcohol intake, physical activity, education level, and income. At the clinic visit, physical examinations were performed including measurement of height, weight, expired carbon dioxide, and forced expiratory volume in 1 second. At each subsequent survey examination, participants were asked whether they were current or past smokers and about duration of smoking (in years). Current smokers were further asked about the usual amount tobacco used in daily cigarettes, cheroots, cigars, and pipes.

Main outcome measure. The primary study endpoint was acute or chronic pancreatitis incidence. Pancreatitis diagnosis and cause of death information was obtained from the Danish Hospital Discharge Register and the Danish Registers of Causes of Death. Information about pancreatitis-related cases among the study participants in these registries was identified through linkage by the unique identification number allocated to every Danish inhabitant by the government.

Main results. Over a mean follow-up period of 20.2 years, 235 cases of pancreatitis occurred. In total, 68% of men and 58% of women were current smokers, and 19% of men and 15% of women were ex-smokers. The researchers observed a dose-response association between smoking and risk of acute and chronic pancreatitis in both men and women. The hazard ratio (HR) of developing acute or chronic pancreatitis was 1.5 (95% confidence interval [CI], 0.9–2.5) for those use used 1 to 14 g of tobacco daily, 2.5 (95% CI, 1.5–3.9) for those who used 15 to 24 g of tobacco daily, and 3.3 (95% CI, 1.9–5.8) for those who used more than 25 g of tobacco daily. Ex-smokers had an HR of 1.7 (95% CI, 1.0–2.7) for risk of pancreatitis. Pack-years of smoking had a similar dose-response relationship to pancreatitis risk. Alcohol intake was associated with an increased risk of pancreatitis (HR, 1.09 [95% CI, 1.04–1.14]) for each additional drink per day. Notably, the risk of acute and chronic pancreatitis associated with smoking was independent of both alcohol and gallstone disease. Overall, 46% of cases of pancreatitis were attributable to smoking in this cohort.

Conclusion. Among Danish men and women followed prospectively for 20 years, smoking was independently associated with increased risk of both acute and chronic pancreatitis in a dose-response fashion.

Commentary

Tobacco use remains the leading cause of preventable death in the United States [1]. The link between tobacco use and lung cancer, cardiovascular disease, COPD, and other cancers is well known. Recent research has linked tobacco to other important diseases, including diabetes [2], and as this study shows, acute and chronic pancreatitis.

The incidence of pancreatitis has increased over the past quarter century and the high associated mortality rate has not decreased [3,4]. Well-known causes of pancreatitis include gallstones and alcohol use. Previous data on smoking as an independent risk factor for pancreatitis are mixed [5–7]. Given the association between both smoking and alcohol use and smoking and gallstone formation, the independent relationship between smoking and pancreatitis may be difficult to disentangle using the case–control research methods that have been commonly used in past studies. However, experimental basic science studies do suggest a relationship between smoking and pancreatic cell damage [8,9].

This study sought to discern in a prospective population-based cohort whether smoking is independently related to

risk of pancreatitis. The investigators report a dose-response relationship between ex-smokers, light smokers, and heavy smokers and increased risk of pancreatitis. These findings expand upon the limitations present in earlier studies that were primarily case–control or flawed cohort studies, and are consistent with the basic science evidence. This current study is notable for its large size, detailed tobacco use questions, and linkage to a central registry of all discharges in Denmark that enabled complete follow-up for all participants. The large size and detailed information on the cohort participant discharge data also enabled the researchers to control for the effects of alcohol use and gallstone disease.

A few limitations to this study deserve mention. The study relied on linkage to a central administrative discharge database based on hospital claims. As such, the data were not clinically verified and only dealt with inpatient visits for pancreatitis, leading to the possibility of misclassification bias and missed outpatient visits for chronic pancreatitis. However, the authors conducted sensitivity analyses to explore these possibilities, without major changes in the results. In addition, external validity may be slightly compromised by the study's location in a small, homogenous Scandinavian country with a very high smoking rate at the time of the study (> 60%).

Applications for Clinical Practice

This large, well-done Danish study suggests that smoking is independently associated with a two- to threefold increased risk for acute and chronic pancreatitis. Clinicians should diligently screen all patients with acute and chronic pancreatitis for tobacco use and use evidence-based cessation methods, including repeated strong advice to quit, telephone quitlines, and medications, to help their patients quit smoking. Current smokers should also be counseled about their increased risk of pancreatitis and be made aware of symptoms that might suggest the onset of pancreatitis for which they should seek prompt medical attention.

—Review by Asaf Bitton, MD

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